REMARKS

Favorable consideration and allowance are respectfully requested for claims 1-10, 12-21 and 23-33 in view of the foregoing amendments and the following remarks.

The Examiner is thanked for the careful review and consideration of this application and for the indication of allowance of claims 13, 15 and 27-32.

Claims 17-21, 23 and 26 have been amended to be in independent form incorporating the limitations of the claim from which they were previously dependant. New claim 33 is directed to a pharmaceutical composition incorporating the compound of formula **Ig** of claim 16.

The rejection of claim 14 under 35 U.S.C. § 102(b) is respectfully traversed. Claim 14 has been amended to remove the compound 5-(4-methoxyphenyl)-1,1,1-trifluoropentan-2-one. Accordingly, claim 14 is believed to be in allowable form. Reconsideration and withdrawal of this rejection are respectfully requested.

The rejection of claims 16 and 25 under 35 U.S.C. § 102(b) over Cailly et al. (EP 0289390) and over Eidenschink et al. (U.S. Patent No. 4,297,515) is respectfully traversed. Claims 16 and 25 have been amended so that they are directed to methods of treating or inhibiting certain conditions rather than being directed to compounds. The Cailly reference teaches the use of certain compounds for the liquid-liquid extraction of radioactivity. The Eidenschink reference teaches the use of certain compounds as liquid crystals. These references do not teach or suggest the claimed methods of treatment. Reconsideration and withdrawal of these rejections are respectfully requested.

The rejection of claim 10 under 35 U.S.C. § 102(b) over Ghomashchi is respectfully traversed. Claim 10 has been amended to incorporate the limitations of previously-pending claim 11. In particular, claim 10 now reflects that the relevant lipase is pancreatic lipase. As indicated in the Office Action,

Ghomashchi teaches a compound to inhibit phospholipases. This reference does not anticipate claim 10, as amended. On page three, the Office Action supports this conclusion, stating that claim 11 was not anticipated by Ghomashchi.

The rejection of claim 11 as obvious over Ghomashchi in view of Johnson et al. (U.S. Patent No. 4,917,826), although moot in view of the cancellation of claim 11, may be relevant to claim 10, as amended. Ghomashchi does not teach or suggest a method for inhibiting pancreatic lipases. The Office Action asserts that Johnson teaches that phospholipases, such as phospholipase A_2 are found in the pancreas. However, phospholipase A_2 is markedly different from pancreatic lipase. The former is neither a substitute for, or equivalent of, the latter.

Pancreatic lipase is a well-established name for the enzymes of Enzyme Classification 3.1.1.3. A synonym for pancreatic lipase is triacylglycerol lipase. Phospholipase A_2, on the other hand, is classified in Enzyme Classification 3.1.1.4. Synonyms for phospholipase A_2 include lecithinase A and phosphatidase.

Differences between the two classes of enzymes are further evidenced by their activities. Only pancreatic lipase targets the outer ester links (positions 1 and 3) of fats in food (fatty acid triglycerides). This renders the enzymes useful in mammalian food digestion. Phospholipase A_2, on the other hand, cannot cleave the outer ester links of fats and instead targets the central ester link (position 2) of phosphatides. Phospholipases preferentially hydrolyze substrates that are located in bilayer membranes, micelles or lipoprotein particles. Accordingly, phospholipases do not play a significant role in the digestion of fat from foods. Phospholipases, like phospholipase A_2, are therefore not suited to reduce the lipid digestion of pancreatic lipase in mammals, particularly humans, to render less usable edible fats. Accordingly, the inhibition of phospholipases does not cause any significant weight loss for patients.

Thus, phospholipases, such as phospholipase A_2, and pancreatic lipase are different, as evidenced by their enzyme classification and their activity. Because

Ghomashchi and Johnson relate to phospholipases, these references are completely different from those of claim 10. The concept of inhibiting pancreatic lipase with the compounds of the present invention is therefore not obvious in view of the cited combination of Ghomashchi and Johnson.

The rejection of claims 1 and 8 as obvious over Ghomashchi in view of Johnson et al. is respectfully traversed.

Claim 1 relates to a method of treating or inhibiting certain conditions by administering certain compounds. Claim 8 further defines the compound used in that method. The Office Action indicates that Ghomashchi fails to teach the treatment or inhibition of the recited conditions. The Office Action then asserts that Johnson teaches that diabetes and obesity can be treated by inhibiting phospholipase A_2. However, Johnson provides no such teaching. As explained below, Johnson provides a wide variety of compounds and then suggests that *some* of them are useful to treat phospholipase A_2 mediated conditions and *some* of them are useful to treat diabetes and *some* of them are useful to treat obesity. There does not appear to be any teaching that a single compound may be useful to treat both phospholipase A_2 mediated conditions and diabetes or obesity.

The Johnson reference maintains the separateness of these conditions throughout. See, for instance, the abstract. The reference never even suggests a connection between diabetes, obesity and the inhibition of phospolipase A_2. For instance, the statement that "[t]he invention also relates to methods of treatment of phospholipase A2 mediated conditions (PMC), and methods of treatment of diabetes, obesity and atherosclerosis, employing the compounds and methods of the invention" clearly shows an understanding that phospholipase A_2 mediated conditions, diabetes and obesity are separate. See col. 7, line 66 through col. 8, line 2.

The reference is generally divided into three separate sections, one devoted to each of phospholipase A_2 mediated conditions, diabetes and obesity. The phospholipase A_2 mediated conditions are particularly discussed in col. 8,

line 3 – col. 10, line 7 and sporadically through col. 11. In col. 12, beginning with line 23, diabetes treatments are discussed and obesity treatments are discussed in col. 13, beginning with line 22. These separate sections appear to reflect the understanding of certain differences between the conditions.

The presence of the words diabetes, obesity and phospholipase A_2 inhibition in a reference does not necessarily mean that the references actually teaches inhibition of diabetes and obesity through phospholipase A_2 inhibition. Examination of the Johnson reference makes clear that the authors were careful to avoid suggesting that diabetes and obesity may be treated through phospholipase A_2 inhibition. The arachidonic acid cascade is suggested as a mechanistic link for the action of certain compounds involved in phospholipase A_2 inhibition. There is no suggestion of such a mechanism for the treatment of either diabetes or obesity. Further the reference teaches that only "*some* of the compounds of the present invention are useful . . . to inhibit phospholipase A_2." See col. 8, line 10 (emphasis added). The reference then indicates that "[*s*]*ome* of the compounds of the present invention are useful as hypoglycemic agents in non-insulin dependent diabetes mellitus (NIDDM) with insulin resistance." See col. 12, lines 23-25 (emphasis added). The reference also states that "[*s*]*ome* of the compounds of the present invention are also useful to treat and/or prevent obesity in mammals including human beings." See col. 13, line 22-24.

Although the reference indicates that phospholipase A_2 inhibitory compounds are useful in the treatment of asthma (see col. 9, lines 58-59), the reference never indicates that the same compounds useful for phospholipase A_2 mediated conditions might be useful to treat metabolic disorders like diabetes and obesity. Diabetes and obesity are not among the cited phospholipase A_2 mediated conditions. As explained above, diabetes and obesity are discussed in separate sections of the reference. Only some of the compounds are useful to treat non-insulin dependent diabetes mellitus (see col. 12, lines 23-39) and some of the compounds are useful to lower serum glucose levels to treat spontaneous

diabetes (see col. 12, lines 40-59). There is no indication of which compounds are effective for which conditions and what features distinguish the effectiveness of the compounds for the different conditions. The reference never states that all of the compounds are useful for any one condition or that even one compound is useful for treating all of the conditions. Further, the reference does not state that the compounds useful for diabetes or obesity would be at all effective to inhibit phospholipase A_2.

Given Johnson's careful distinction between the metabolic conditions (diabetes and obesity) and the phospholipase A_2 mediated conditions, one of skill in the art would not understand that compounds effective for treating the metabolic conditions might also be effective to inhibit phospholipase A_2. Johnson provides no teaching or suggestion to try to use compounds effective for treatment of obesity or diabetes in the treatment of phospholipase A_2 mediated conditions. In fact, one of skill in the art would likely conclude that because only some compounds are useful to treat the metabolic conditions and only some compounds are useful for the phospholipase A_2 mediated conditions, these conditions do not share a common mechanism. Accordingly, one of skill in the art would likely conclude that other mechanisms for treating phospholipase A_2 mediated conditions would similarly not be useful in treating the metabolic conditions.

Thus, Johnson does not teach that diabetes and obesity can be treated by inhibiting phospholipase A_2. For these reasons, the reference provide one of skill in the art with no motivation or guidance to try to combine the teachings of Johnson with Ghomashchi. Reconsideration and withdrawal of this rejection are respectfully requested.

CONCLUSION

In view of the foregoing, the application is respectfully submitted to be in condition for allowance, and prompt favorable action thereon is earnestly solicited.

If there are any questions regarding this response or the application in general, a telephone call to the undersigned would be appreciated since this should expedite the prosecution of the application for all concerned.

If necessary to effect a timely response, this paper should be considered as a petition for an Extension of Time sufficient to effect a timely response; please charge any deficiency in fees or credit any overpayments to Deposit Account No. 05-1323 (Attorney Docket No. 029300.52994US).

Respectfully submitted,

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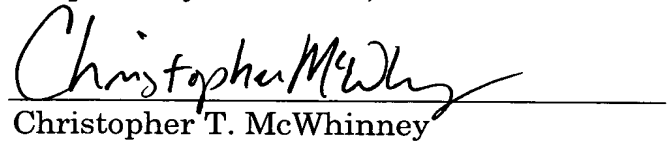

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